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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Mr. Maurice Mermey, Director of the Bureau of Education on Fair Trade and Professor Louis B. Schwartz of the University of Pennsylvania on the occasion of their debate on Fair Trade, April 24, 1957

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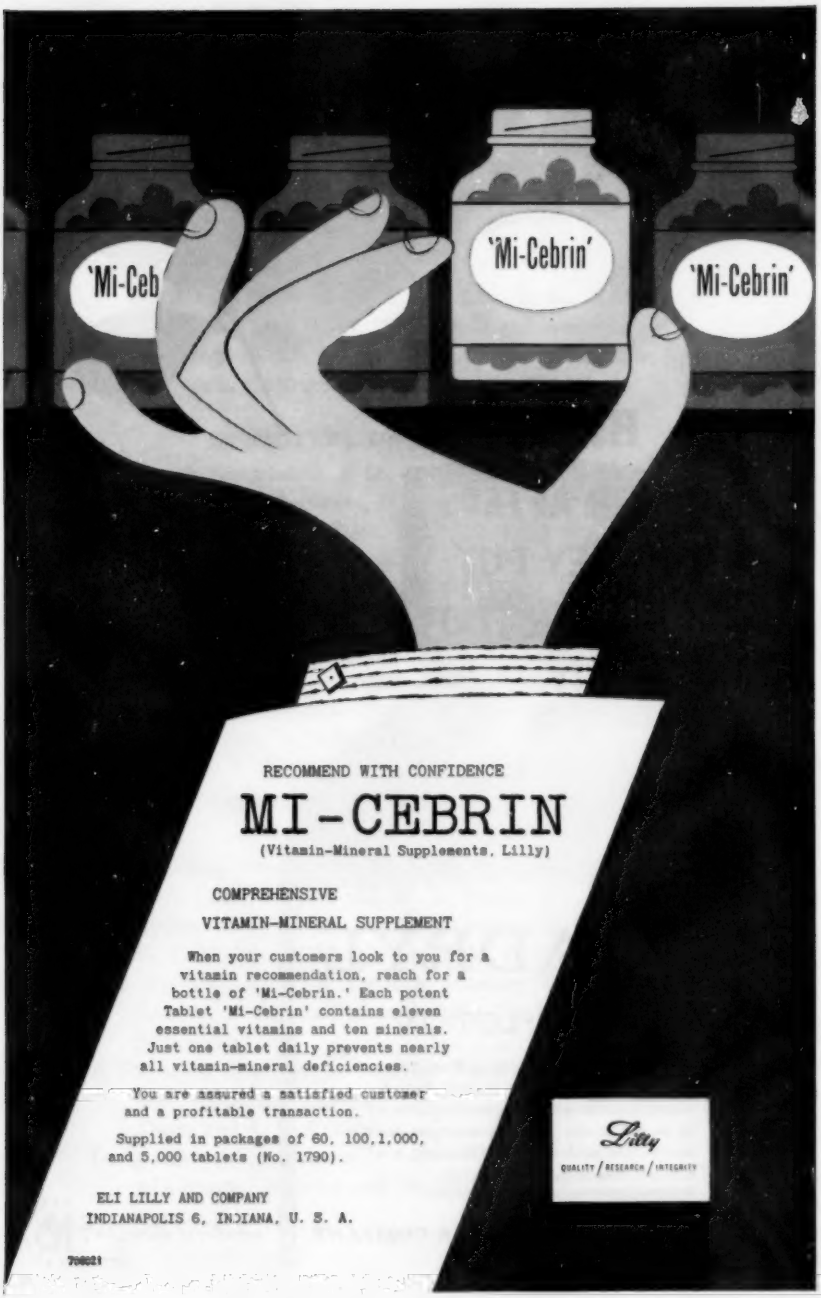

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CONTENTS

EDITORIAL

CONSUMER SUPPORT FOR FAIR TRADE

THE attack on resale price maintenance continues at both the state and national level. Already, the battle has been lost in several states and we can be sure that these victories will only intensify the vigor of our opponents.

While few retail pharmacists can be found who do not believe in fair trade, far too few work as diligently in protecting themselves against its loss and supporting those manufacturers who work with them in maintaining the fair trade structure.

It is not our purpose here again to reiterate the basic principles of fair trade, why they can be justified, and why resale price maintenance is necessary for the protection of trade-marks in the manufacturers' interests. These facts are well-known to pharmacists, just as the chaos which took place in the days before fair trade is still vividly remembered. The purpose of this editorial is to drive home a point almost never given the attention and consideration it deserves. This is that fair trade legislation cannot be preserved by political pressure alone, applied by pharmacists and others engaged in retail selling. If fair trade is maintained, it is absolutely essential that the philosophy behind it be not only understood but accepted and endorsed by the consuming public. Time and time again, the consumer becomes almost violent in his opposition to the structure which prevents some merchant from selling him merchandise which he, the consumer, wants at a price far below the prevailing level. Consumers, invariably, are price conscious and, in order for them to pay more for something than might otherwise be necessary and do this without protest, some very solid explanation must be forthcoming. They are not in the least impressed with the statement that fair trade operates in the interest of the manufacturer and the retailer. Arguments which have meaning must show how fair trade is helpful to them as individuals. This is not an easy task for they must be shown that, in the long run, spending more for a given product at a given time is economical and protects their interests as consumers. There are some telling arguments which can be used.

It can easily be shown that our great purchasing power, our high standard of living, and the quality products which we can buy depend basically on our free enterprise system, which in turn is completely dependent upon the continued existence of the small business man and his economic welfare. There are many other arguments known quite well to one who is genuinely interested in fair trade and which should be used on every occasion.

While our legislators are fully aware of the position of influence which we as pharmacists occupy with respect to public opinion, they are also quite sensitive to the wishes of the public at large. This, they must be if it is their aim to remain in office. Although they may themselves believe in fair trade and want desperately to support us in our position, they can only do it if the great bulk of public opinion is favorable. This is the job which we must accomplish rather than expect our legislators to force it down the throats of a protesting public.

Pharmacists and all others engaged in retail activities must work more diligently in this direction if the tide of battle is to be turned. Old-timers who remember the pre-fair-trade days should draw this specter for their younger associates, and all should make the proper influencing of public opinion a part, and an important part, of their daily activities and public relations.

L. F. Tice

A SIMPLIFIED, POWDERED, WASHABLE OINTMENT BASE.[1]

By James A. Lee,* Phyllis Caver ** and W. Lewis Nobles ***

IN the past several years, considerable attention has been devoted to the development of hydrophilic ointment bases, otherwise termed "washable" ointment bases. Such preparations possess the advantage of being non-greasy, pleasant in appearance and easily removed by washing with water. Since in the more solid types of dermatological preparations, such as ointments, the concentration of the medicament rarely exceeds 10%, it is evident that the vehicle to be used will definitely constitute the larger part of the preparation.

Zopf (1) has delineated certain criteria which a satisfactory ointment base should possess:

1. Washability
2. Low index of irritation
3. Compatibility with most agents used in dermatology
4. Efficient release of the medicament at the site of application
5. Stability
6. Ease of preparation

To these, Sperandio (2) has recently added the suggestion that it should be composed of a powder of such nature that pharmaceutically elegant preparations might be formed by the simple addition of water, followed by agitation. Zopf (1) had previously indicated that this should be an ideal for the most suitable type of dermatological vehicle.

Previously, we (3) had reported on the use of Carbopol 934 [2] as a dermatological vehicle. It was pointed out that a base of this

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[1] This project was supported by a research grant from the B. F. Goodrich Chemical Company.

[2] Product of B. F. Goodrich Chemical Company.

synthetic hydrophilic colloid was compatible with 13 medicinals commonly prescribed in dermatological medication. In this initial work, the base was prepared from the synthetic acid polymer by neutralizing an aqueous dispersion of the polymer with a suitable alkaline agent such as sodium carbonate. Although the ointments were very satisfactory, this method of preparation was made somewhat tedious by the necessity of maintaining a solution of the neutralizing agent of the proper percentage strength or of weighing out the quantity of neutralizer at the time of preparation.

We should now like to report a method for the use of this same base in compounding an ointment base that meets the general criteria for ointment bases and, in addition, is composed of only *one* substance which will yield a satisfactory ointment simply by the addition of water to the polymer salt blended with the desired medicament, followed by suitable agitation. This method involves the use of a preneutralized form of Carbopol 934.

Carbopol 934 is normally available as an acid polymer which may be neutralized to form a clear stable gel. Shortly after the work previously cited (3) was completed, a technique was made available for the preparation of mucilages from this agent utilizing an aqueous-alcoholic slurry. This made use of the fact that while Carbopol 934 is soluble in alcohol in the acid state, the polymeric salts are quite insoluble in this vehicle. Thus, a slurry formed from Carbopol and a methanolic-aqueous solution of sodium hydroxide could be added to a formulation to give the desired thickening. Since the polymeric salts were insoluble in this vehicle, this afforded a possible means of utilizing the dry salt of the polymer. This was accomplished in the following manner: A slurry was prepared in the manner described in the company bulletin (4). The slurry thus obtained was filtered through a Buchner funnel to yield an adhesive white mass. This solid was dried for approximately 1½ hours at 125° C. It was then reduced to a fine particle size by means of high speed agitation in a Waring blendor.

A satisfactory gel may be obtained rather quickly by rapidly agitating 1-5% of this salt in water. The gel obtained by dispersing 5 Gm. of the salt in 95 ml. of water has a pH of 6.8.

Utilizing the dried sodium salt of Carbopol, ointments containing the same dermatological medicaments previously reported (3) were prepared in the following manner: The medicament, if solid,

was dry blended with the desired quantity of the sodium salt of Carbopol. (Suitable concentrations are indicated in Table I.) This may be done on a small scale with the aid of the mortar and pestle; on large runs, a Patterson-Kelley yoke model blendor was utilized. To the mixture of the dry powders was then added slowly, with agitation, the calculated amount of water necessary to prepare the ointment.

In each case, the ointments were easily compounded, elegant in appearance and stable at room temperature throughout the test periods employed. The ointments were observed at the following time intervals:

1. Immediately after preparation
2. Seven days after preparation
3. Thirty days after preparation
4. Ninety days after preparation

In no case was there any evidence of changes in the ointments thus prepared. A list of the ointments prepared in this manner is indicated in Table I.

TABLE I

OINTMENTS PREPARED WITH THE AID OF THE SODIUM SALT OF CARBOPOL 934

Medicament	% Carbopol Salt Used
Boric Acid 10%	5
Ichthammol 10% *	6
Ammoniated Mercury 5%	2
Benzoic Acid 12% Salicylic Acid 6%	5
Coal Tar 5%**	10
Iodine 5% ***	6
Sulfur 10%	5
Histadyl Hydrochloride 2%	2
Penicillin (1000 units/Gm.)	5
Achromycin Hydrochloride 3%	5
Benzocaine 1%	2

* The Ichthammol was dissolved in a minimum amount of water and this solution was added to the dry salt.

** The coal tar was mixed with polymer salt by trituration and then water was added slowly with agitation.

*** The iodine was dissolved in an aqueous solution of KI. This solution was then added to the Carbopol salt.

In addition to this agent serving as an extremely efficient thickener in formulations of this type, additional information is now available relative to its toxicity. In brief, it may be stated that the toxicity of 934 is negligible (5). Insofar as dermatological preparations are concerned, its safety is indicated by the fact that in tests employing up to 200 people, both male and female, no irritation or sensitization was demonstrated when it was patch tested in either of the following manners:

1. Continuous exposure for five days with reapplication for forty-eight hours after three weeks.

2. Exposure every other day for thirty days with reapplication for forty-eight hours after three weeks.

Summary

Twelve commonly prescribed dermatological medicaments have been incorporated into a base composed of the sodium salt of Carbopol 934 and water. The dry medicaments were blended with the salt and then the ointments were prepared by the addition of water with agitation.

Thus, an ointment base consisting of a single chemical from which ointments may be prepared by the addition of water, followed by agitation, without the necessity of heat, is herein described.

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ABSORPTION OF ENZYMES FROM THE INTESTINAL TRACT.

By Gustav J. Martin, R. Brendel and J. M. Beiler *

TRYPSIN has been shown to exert an anti-inflammatory action in the laboratory (1) and clinic (2) when it is administered buccally. These findings have been interpreted as indicating that the increase in tissue permeability produced by the enzyme (3) was sufficient to facilitate its passage through membranes which it might normally not be expected to penetrate because of its large molecular size.

In view of the clinical implications, it seemed a logical extension of these findings to investigate the possibilities of absorption from the intestinal tract of enzymes which were known to affect permeability. Accordingly the effects of a number of proteolytic enzymes which had been shown to have anti-inflammatory action (4) and to produce permeability increases (3, 5) were investigated.

Experimental

Effects on egg-white edema were taken as a measure of extent of absorption from the intestinal tract. All the enzymes tested had been shown (4) to inhibit this experimental edema after subcutaneous or intraperitoneal administration. The edema was produced in rats about 100 grams in weight by injection of egg-white into one leg, as previously reported (4).

In one series of experiments, the enzymes tested were injected directly into the ileum, in order to avoid the possibility of their inactivation in the upper portion of the intestinal tract by the digestive ferments. Animals were anesthetized by intraperitoneal administration of chloretone, 200 mg./K. Abdominal incisions were made and the enzymes, in 0.5 ml. of saline, injected directly into the exposed intestine. The incisions were stitched and egg-white was injected into the plantar surface of one hind paw 40 minutes after administration of the enzyme. The animals were sacrificed 90 minutes after

* The National Drug Company, Philadelphia, Penna.

injection of the egg-white and the weights of the inflamed and normal legs determined. Control groups were treated identically, except that injections into the intestine consisted of 0.5 ml. of saline alone.

Experiments on direct oral administration were done only with trypsin. The enzyme was administered either in 0.5 ml. of saline or in 0.5 ml. of an emulsifying mixture consisting of Span 80, 20 per cent by volume and corn oil 80%. Tragacanth 5% and gelatin 22% were also used as vehicles. In these experiments it was felt that rate of absorption of the enzyme from the viscous carriers might be a factor which would influence the results. Preliminary work established that no significant differences were obtained with pretreatment times ranging from one to three hours. The latter time was adopted as routine, and in the experiments reported trypsin was administered orally three hours before the injection of egg-white. Animals were sacrificed 90 minutes after this injection and the extent of the edema determined.

Results

Table I gives the inhibitory effects on egg-white edema of various enzymes injected directly into the ileum. Figures were obtained (4) by comparing the weight differences between the egg-white and saline-injected legs of the enzyme-treated animals with those of controls. All figures are averages for groups of six animals. Inhibitory effects reported were established by rank analysis to be significant within the $P = 0.05$ range.

TABLE I

Inhibition of Egg-White Edema by Enzymes Injected Into the Ileum

Enzyme	Dose (mg/K)	Inhibition of Edema (per cent)
Trypsin	20	48
Chymotrypsin	20	39
Prolase-B	20	32
Streptokinase	20	0
Streptokinase	50	32
Papain	50	17

In Table II are presented the results obtained on direct oral administration of trypsin in various vehicles. Figures are averages for groups of twelve animals, significant within the $P = 0.05$ range.

TABLE II

ANTIPHLOGISTIC EFFECT OF ORALLY-ADMINISTERED TRYPSIN

Dose (mg/K)	Vehicle	Inhibition of Edema (per cent)
500	Saline	0
200	Tragacanth 5%	0
200	Gelatin 22%	0
200	Emulsifying mixture	37
100	Emulsifying mixture	30
50	Emulsifying mixture	0

Discussion

All the enzymes tested showed definite inhibitory action on the experimental edema on inter-ileal administration. It is interesting to note that the same relative activities obtain as were found on parenteral administration. Both Streptokinase (as the commercial preparation Varidase) (4) and papain (6) have been found to be inferior on a weight basis to crystalline trypsin and chymotrypsin as antiphlogistic agents. The absorption of these enzymes from the intestinal tract may be a function of their effects on permeability. Such an explanation may not apply to streptokinase, which has no direct proteolytic action. However, the preparation used is known to be impure, and to contain substances which do exert effects on permeability. Absorption of streptokinase, therefore, may have been facilitated by impurities.

On direct oral administration, trypsin showed a marked antiphlogistic effect when it was prepared in an emulsifying mixture. Since the enzyme in saline and the other vehicles used was inactive, it would appear that the emulsifying mixture made possible the formation of a water-in-oil emulsion which protected the trypsin from the action of the intestinal digestive enzymes. This protection would seem not to have been complete, since effective doses of trypsin administered by this method were appreciably higher than those required when the enzyme was injected directly into the ileum, thus by-passing

the zone of greatest concentration of digestive enzymes. The possibility of poor absorption from a water-in-oil emulsion must also be considered in attempting to account for the quantitative differences obtained.

The results indicate the possibility of clinical administration of proteolytic enzymes by the oral route. Theoretically enteric-coating should provide protection from the action of intestinal enzymes and allow the absorption of the proteolytic enzymes and the exercise of their systemic anti-inflammatory effects. Dosage might have to be higher than that now used for parenteral administration, but this would be more than compensated for by the convenience of the oral route.

Summary

A number of proteolytic enzymes have been shown to inhibit the development of experimental edema after administration in the intestinal tract. The effect occurs when the enzymes are protected from digestive action either by injection directly into the ileum or by incorporation into an emulsifying mixture.

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THE APPLICATION OF THE PALISADE NUMBER METHOD TO THE LEAVES OF ALEXANDRIA AND INDIAN SENNA

By Harold I. Silverman *

IN a previously published paper (1), a method employing comparative palisade number counts was introduced and defined as a means of identifying the leaves of spearmint and peppermint. This method was successful in the cases tried, and was also adapted to the quantitative determination of these two drugs when in powdered admixture (2).

Cassia angustifolia Vahl and Cassia actuifolia Delile are microscopically differentiated (3, 4) by somewhat difficult techniques. These techniques are based upon number and length of trichomes, number of stomata with counts on their neighboring cells, palisade ratio determinations and vein islet numbers. The palisade ratios of these drugs are too close to each other to be of value in their differentiation (5), while the other methods mentioned are tedious and difficult for the inexperienced worker (6).

The palisade tissue of the mesophyll of senna leaves occurs on both the upper and lower surfaces of the blade and is well defined in both (6). Since by means of palisade number counts, the leaves of spearmint and peppermint were readily identified it was thought that by applying this counting method to both the upper and lower epidermis of the isolateral leaf of senna numerical data would be accumulated that might prove valuable for species differentiation.

Method and Materials

The method employed was similar to that described in a previous paper (1), differing only in that both the upper and lower palisades of both Alexandria and Indian senna were used for the palisade number counts. In all, twelve different sources of each drug were examined, samples being obtained either from herbaria or commercial sources. These were carefully rechecked, in each case, for authen-

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ticity both by comparison with known material and conforming with descriptions set forth in standard botanical keys. The leaves examined ranged in size from 0.5 cm. to 1.5 cm. in width and from 2.0 cm. to 4.5 cm. in length. Only entire unbroken leaves were selected for this study. Figures 1 to 16 illustrate the appearance of the palisade cells of Alexandria and Indian senna in each of the respective positions selected for the counts.

Each small rectangle of the Howard Micrometer Disc measured 55 microns per side when using a magnification of 430 diameters.

UPPER LAYER PALISADE TISSUE

ALEXANDRIA SENNA

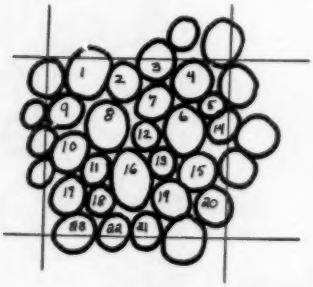

FIG. 1
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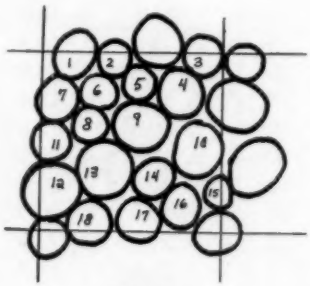

FIG. 2
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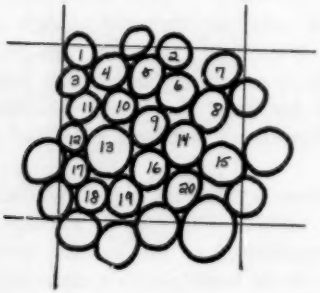

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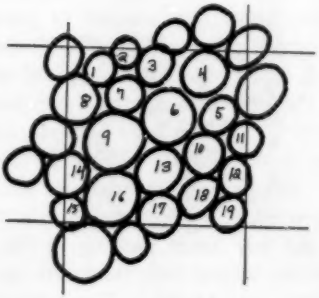

FIG. 4
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Data and Conclusions

The data obtained in computing the palisade number counts are given in Table 1.

TABLE 1

PALISADE NUMBER COUNTS—SENNA LEAVES

	Upper Mesophyll			Lower Mesophyll	
	Alexandria	Indian		Alexandria	Indian
1	14.3	13.1		14.3	9.8
2	15.0	15.1		15.1	10.1
3	16.9	15.4		15.8	10.9
4	17.1	16.6		15.9	11.1
5	17.6	16.8		16.4	11.9
6	17.8	16.8		16.6	14.3
7	18.6	17.1		17.3	16.3
8	19.0	17.5		18.0	16.5
9	19.5	20.1		18.1	17.2
10	19.8	20.6		18.1	17.3
11	20.4	20.9		18.6	17.9
12	21.5	22.9		19.1	19.9
	18.1	17.7	Average	16.9	14.4

Two counts were performed for each position selected on the leaf, both for the upper and lower epidermis. Each value represents the average number of palisade cells that occurred in each of the small rectangles of the Howard Micrometer Disc for each leaf. This figure was based on eight separate counts of the palisade cells in the unit area of the Micrometer for each leaf in the positions taken (1). The total palisade number counts executed were therefore three hundred and eighty-four.

It can be noted that in both senna species the dorsal palisade has a slightly lower count than the upper. This can be attributed to the less dense packing in the organization of this cellular layer and the consequently larger air spaces in the lower palisade mesophyll, (Figs. 5-8; 13-16). This appears to conform with the well-known phenomenon of stronger development of leaf tissue in that part of the leaf receiving the most light (7).

When the average palisade number counts of both Alexandria and Indian senna were compared it was evident that there existed no significant difference in the upper palisade, while in the lower palisade a small variation did occur. This latter difference is unfortunately insufficiently large to permit ready identification of these two drugs as separate from one another if palisade number counts were used solely as the method for determination of species.

LOWER LAYER PALISADE TISSUE

ALEXANDRIA SENNA

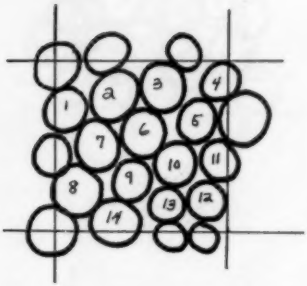

FIG. 5
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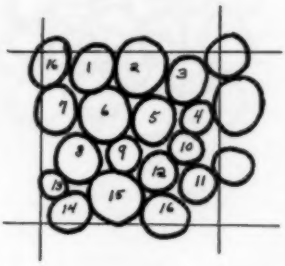

FIG. 6
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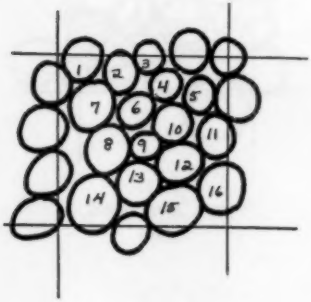

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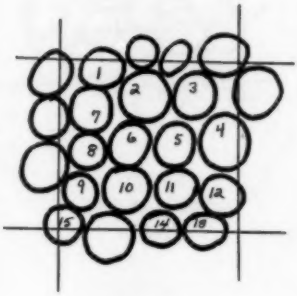

FIG. 8
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UPPER LAYER PALISADE TISSUE

INDIAN SENNA

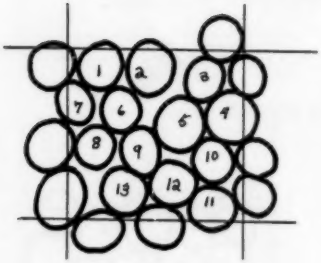

FIG. 9
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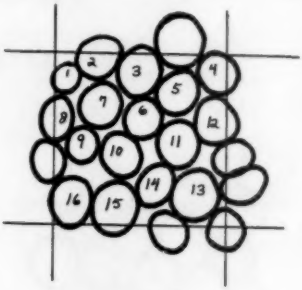

FIG. 10
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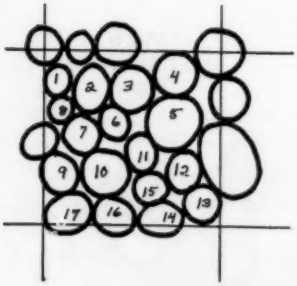

FIG. 11
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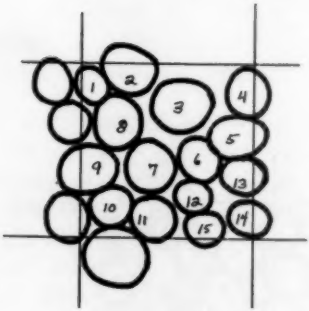

FIG. 12
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LOWER LAYER PALISADE TISSUE
INDIAN SENNA

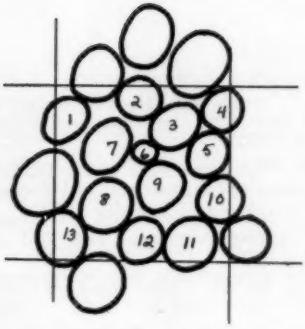

FIG. 13
APPX. MAG. 480X
TIP

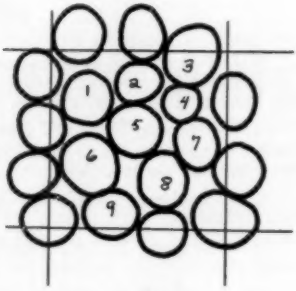

FIG. 14
APPX. MAG. 480X
MIDRIB

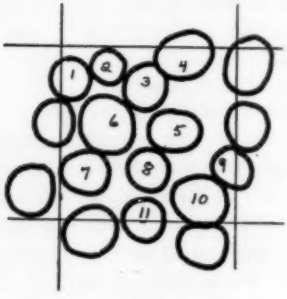

FIG. 15
APPX. MAG. 480X
BASE

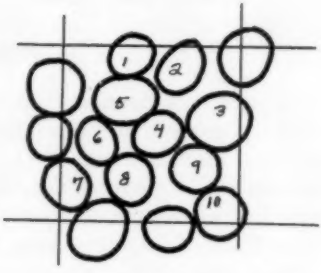

FIG. 16
APPX. MAG. 480X
SIDE

REFERENCES

(1) Silverman, H. I. and Dunn, M. S., "Comparative Palisade Numbers as a Means of Microscopically Separating and Identifying Peppermint and Spearmint Leaves," *Am. Jour. Pharm., 128:*19-23 (1956).

(2) Silverman, H. I. and Dunn, M. S., "The Application of the Palisade Number Method to the Quantitative Determination of Spearmint and Peppermint when in Powdered Admixture," *Am. Jour. Pharm., 128:*98-101 (1956).

(3) Schneider, A., *Microanalysis of Powdered Vegetable Drugs,* 2nd ed., Phila., Blakiston, 1921, p. 167.

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(6) Wallis, T. E., *Pharmacognosy,* 3rd ed., London, J. & A. Churchill Ltd., 1955, pp. 135-136.

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A STATISTICAL STUDY OF THE PALISADE NUMBERS OF PEPPERMINT AND SPEARMINT LEAVES.

By Harold I. Silverman *, Marin S. Dunn ** and Joseph L. Ciminera ***

IN a recently published paper (1), the term palisade number was introduced and defined as an aid to microscopically identifying and separating the leaves and leafy fragments of peppermint and spearmint. This work was extended (2, 3), to quantitative determinations of these drugs when admixed with each other and in combinations with other selected Labiatae.

Using statistical methods, the palisade numbers determined for peppermint and spearmint have been analyzed and an interpretation made. This has been done with the realization of the increasing importance that statistics is playing in biological work to furnish a sounder basis for the interpretation of data. The analysis has been carried out on all four leaf positions selected for the palisade number counts and their average.

Drug Sources

Material examined comprised herbarium sheet specimens, commercial samples and plants grown especially for this study. Herbarium sheets bore the name of a prominent collection or were initialed by experts. In the case of commercial samples, the material was sent by the suppliers with the statement that it had been authenticated by them, or in some cases, the drug containers bore either the U. S. P. or the N. F. label. In reference to the freshly grown samples,

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some were raised in a botanical garden and were labeled as being authentic species. Others were greenhouse plants grown by specialists and were labeled as authentic specimens. All of this material was examined in our laboratories before use and the identification of the respective species confirmed, as well as possible, by comparison with characteristics such as petiole length, serration and hairiness set forth in standard botanical keys.

Data

Tables 1 and 2 record the palisade numbers of peppermint and spearmint leaves that were selected from the accumulated data for statistical analysis. In some cases where more than one leaf was examined from the same lot, one leaf was selected and the other(s) rejected using a table of random numbers. Both larger (over 1.5 cm. in length) and smaller (less than 1.5 cm. in length) leaves were used. None of the smaller leaves measured less than 1.25 cm. in length. Only entire leaves were used for the statistical study. Portions of the leaves were not included. Table 3 shows the results of the statistical analysis. The resultant "F" values were tested for significance by comparing with tabulated "F" values at the 0.05, 0.01 and 0.001 probability levels. Table 4 shows the mean counts and differences between peppermint and spearmint for the various leaf positions in the unit area of the Howard Micrometer Disc selected.

Discussion and Summary

Using statistical methods an attempt has been made to answer the following:

1. Is there a significant difference between peppermint and spearmint leaves which can be determined by noting their respective palisade numbers?

2. Is there a significant difference among the positions chosen on the leaf for the palisade number counts, (tip, midrib, base and side)?

3. Is the difference in palisade numbers between peppermint and spearmint leaves consistent among the four leaf positions?

From the study of the data recorded and evaluated, the following observations appear evident:

(a) The average count for spearmint was 18.5 palisade cells in the unit area selected of the Howard Micrometer Disc. The average count for peppermint leaves was 9.1 palisade cells in this same unit area. The difference of 9.4 cells was highly significant statistically ($P \langle\langle 0.001$—i.e., there is less than one chance in a thousand that a difference of this magnitude might have occurred by chance alone, if there were no real difference in count).

(b) There was some evidence ($P \langle 0.05$) that there might be slight differences in count with different leaf positions. Specifically, there was a tendency for the tip count for spearmint to be slightly lower than for the other leaf positions, and for the base count to be slightly higher for both peppermint and spearmint. However, these differences were trivial and had no great bearing on the problem.

(c) The analysis indicated also that there was no significant interaction between leaf positions and type of leaf. This means that the difference in palisade count between peppermint and spearmint was consistent, within limits of error, at all four leaf positions studied.

(d) The 95% confidence limits for the difference in mean palisade number were 7.6 and 11.2($= 9.4 \pm 1.8$) cells per unit area. This means that if a similar experiment were repeated a large number of times, we would expect to find the average difference in count between the two drugs to be between 7.6 and 11.2 cells in 95% of the trials.

This method is now being extended (4) to other leafy drugs (which are presently differentiated only with difficulty) in hopes that it will prove to be of further value.

TABLE 1

PALISADE NUMBERS OF PEPPERMINT LEAVES SELECTED FOR STATISTICAL ANALYSIS

Leaf No.	Tip	Midrib	Base	Side
1	10	10	13	11
2	11	10	9	10
3	6	7	5	7
4	9	10	10	9
5	12	13	15	14
6	12	9	11	8
7	9	9	10	8
8	7	8	8	8
9	11	10	11	10
10	11	10	11	10
11	10	9	9	11
12	11	10	9	11
13	6	6	7	8
14	7	7	7	6
15	7	7	9	7
16	8	8	9	9
17	11	9	13	10
18	7	6	7	7
19	11	11	11	14
20	7	10	11	9
21	7	5	8	7
22	6	7	6	6
23	10	12	11	9
24	10	10	8	11
Total	216	213	228	220
Average	9.0	8.9	9.5	9.2

TABLE 2

PALISADE NUMBERS OF SPEARMINT LEAVES SELECTED FOR STATISTICAL ANALYSIS

Leaf No.	Tip	Midrib	Base	Side
1	22	20	18	22
2	14	12	14	13
3	25	20	32	24
4	23	18	22	20
5	21	24	29	23
6	16	17	17	18
7	14	21	21	20
8	20	21	30	20
9	14	18	17	16
10	23	24	24	25
11	25	22	21	23
12	19	18	18	21
13	18	21	18	19
14	14	17	16	17
15	18	18	19	18
16	17	22	20	17
17	16	23	18	21
18	12	13	12	12
19	22	21	20	19
20	18	19	22	21
21	23	23	24	24
22	13	13	10	12
23	11	14	16	14
24	13	16	14	14
25	10	11	12	10
26	14	14	15	13
27	18	18	19	21
28	19	21	20	23
Total	492	519	538	520
Average	17.6	18.5	19.2	18.6

TABLE 3

ANALYSIS OF VARIANCE[1]

Source of variation	D. F.	S. S.	M. S.	F(obs)	F(tab)
Among leaves	51	6594	129		
Spear. vs. Pepp. (T)	1	4507	4509	107.33***	.001 12.3
Leaves in T (error a)	50	2087	41.74		
Within leaves	156	474	3		
					.01 3.91
Position on leaf (P)	3	33	11	3.67*	.05 2.67
P x T interaction	3	11	4	1.33	.05 2.67
P x leaves in T (error b)	150	430	2.87		
Total	207	7068			

*** Highly significant, $P < 0.001$.

* Significant, $P < 0.05$.

1. Snedecor, Statistical Methods (5th ed.; Ames, Iowa: Iowa State College, Press, 1956), p. 366.

TABLE 4

TABLE OF MEANS

	Tip	Midrib	Base	Side	Over-all average
Spearmint	17.6	18.5	19.2	18.6	18.5
Peppermint	9.0	8.9	9.5	9.2	9.1
Difference	8.6	9.6	9.7	9.4	9.4

REFERENCES

(1) Silverman, H. I. and Dunn, M. S., "Comparative Palisade Numbers as a means of Microscopically Identifying and Separating Peppermint and Spearmint Leaves," *Am. Jour. Pharm. 128:*19-23 (1956).

(2) Silverman, H. I. and Dunn, M. S., "The Application of the Palisade Number Method to the Quantitative Determination of Spearmint and Peppermint when in Powdered Admixture," *Am. Jour. Pharm. 128:*98-102 (1956).

(3) Silverman, H. I. and Dunn, M. S., "The Determination of the Relative Percentages of Selected Members of the Labiatae, in Various Powdered Admixtures," *Am. Jour. Pharm. 128:*225-234 (1956).

(4) Mason, C. W., Personal Communication: College of Engineering, Cornell University, Ithaca, N. Y.

DRUG INFORMATION SOURCES *

(Denmark, Norway and Sweden)

DENMARK

Danmarks Apotekerforening. **Specialitetstakst 1956.** 8th ed. Copenhagen, The Association, 1956. 438 pp. 45.00 Kr.

Specialitetstakst is the pharmaceutical association's list of specialties manufactured or sold in Denmark. Composition, manufacturer, forms supplied, price and reference to pricing and prescribing regulations are given for individual drugs listed. The number assigned to each drug by the State Board of Health is also included. There are also lists of manufacturers and Danish representatives of foreign manufacturers with their addresses. *Specialitetstakst* is supplemented by detachable leaves in *Archiv for Pharmaci og Chemi* (biweekly). The Association's address is Hammerichsgade 14, Copenhagen V.

Sundhedsstyrelsen. **Fortegnelse over Medicinske Specialiteter og Mærkevarer Optaget i Sundhedsstyrelsens Specialitetsregister.** 1st ed. Copenhagen, H. P. Hansen's Bogtrykkeri, 1956. 169 pp. Free.

This is the State Board of Health's list of specialties sold in Denmark. Manufacturer's name, forms supplied and package sizes are given for individual drugs, but not prices. It is supplemented by detachable leaves in the biweekly *Archiv for Pharmaci og Chemi*. Publisher's address: Holbergsgade 20, Copenhagen K.

NFN-Navne. Copenhagen, Nyt Nordisk Forlag Arnold Busk, 1950. 55 pp.

A one-volume summary of non-proprietary names determined by Nordiske Farmakopé-naevn. The text is arranged in four sections: I, Principles of nomenclature. II, Names accepted and used in Nordic pharmacopeias. III, Names not included in Nordic phar-

* A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

macopeias. IV, Alphabetical list of synonyms including the source of the name (i.e., pharmacopeia, trade name) and suggested NFN name. Names of Norway, Sweden, Denmark, Finland and Iceland are included. It is supplemented by lists in current Scandinavian journals. A new edition has been announced for the latter part of 1957. Publisher's address: Koebmagergade 49, Copenhagen K.

Danmarks Apotekerforening. **DAK Praeparater.** 7th ed. Copenhagen, H. P. Hansen's Bogtrykkeri, 1951. 2 volumes. 25.00, 6.00 Kr.

A loose leaf formulary compiled by Danmarks Apotekerforening. Volume 2 is *Codex Medicamentarius Scandinavicus*. Dosage is given, as well as formulas. Publisher's address: Holbergsgade 20, Copenhagen K.

Farmakopekommissionen København. **Pharmaconomica Danica.** 2d ed. Copenhagen, Nyt Nordisk Forlag Arnold Busk, 1954. 252 pp. 6.85 Kr.

A pocket-size alphabetic list of drugs under their latinized names, in which are given synonymous names, composition, action, indications, maximum dosage and prescription status. A section on antidotes to poisons and an index by principal constituent or action are also included. There is a general alphabetic index to Danish names. Publisher's address: Kobmagergade 49, Copenhagen K.

Medicamina Nova 1956. Copenhagen, Nordisk Medicin, 1956. 124 pp. 7 Kr.

A compilation of monographs on current medicinals. Entries give information about composition, action, indications, dosage and manufacturer. Monographs have previously been published in issues of *Nordisk Medicin*. Publisher's address: P. Hvitseldtsstraede 9, Copenhagen K.

Laegeforeningens Aarbog 1957, Afd. 1: Lommebog. 42nd ed., by Mogens Fog. Copenhagen, N. Olaf Møller, 1956. 530 pp.

In this annual compilation drugs are arranged in groups according to their effects. Within each group they are listed alphabetically.

The text supplies information about composition, action, indications, dosage, manufacturer, forms supplied and price of individual drugs. Publisher's address: Frederiksborggade 26, Copenhagen K.

Veterinære Sundhedsrad. **Dispensatorium Veterinarium 1950.** Copenhagen, Gyldendalske Boghandel-Nordisk Forlag, 1950. 181 pp.

A formulary of drugs used in veterinary practice. Drugs are entered alphabetically by Latin name. Entries give Danish name, formula, directions for compounding and dosage. The general alphabetic index includes all drug names.

NORWAY

Norges Apotekerforening. **NAF Boken; Norges Apotekerforenings Formelsamling 1952.** Oslo, A. W. Brøggers Boktrykkeri, 1952. N. kr. 55.

This formulary compiled by the pharmaceutical association gives formulas and details of methods to be used by pharmacies in their production departments. Drugs are entered alphabetically by Latin name, followed by Norwegian name. Cosmetics and reagents are included, as well as medicinals. All significant drug names appear in the general alphabetic index. No proprietary names are mentioned. New formulas are supplied irregularly in loose leaf binders. A new edition is expected in 1960. The Association's address is Arbiens Gate 3, Oslo 21.

Norsk Formelsamling 1953 (Formulae Norvegicae (F. N.)). 3d ed., compiled by Jens Bjørneboe and Tor Christiansen. Oslo, A. W. Brøggers Boktrykkeri, 1953. 362 pp.

Drugs are entered alphabetically by Latin name and common names are also included. The formulas are brief in comparison with NAF-Boken, but entries include a statement of indications and frequently dosage and method of administration. A therapeutic index and an index by principal constituent, as well as a table of maximal dosages and a section on antidotes to poisons are included.

Spesialitetstakst, edited by Elias Reite. Norges Apotekerforening. Oslo, A. W. Brøggers Boktrykkeri, 1956. 250 pp. N. kr. 100, including supplements.

Spesialitetstakst is a comprehensive alphabetic list of pharmaceutical specialties manufactured or distributed in Norway. Entries give for individual drugs their composition, manufacturer, sizes issued and price. Each drug has a number which refers to its group in the separate therapeutic index. There are also a list of manufacturers with their addresses and a list of NFN (Norge Farmokopénaevn) names. Price corrections and lists of new preparations appear monthly and complete revision occurs every two years. The Association's address is Arbiens Gate 3, Oslo 21.

Farmatek. Oslo, A/S Farmaceutisk Industri. Cards 4⅛″ × 5⅞″. N. kr. 15 per year.

This card service of pharmaceutical specialties includes drug preparations registered in Norway. Drugs are entered by proprietary name. Information for individual products includes composition, indications, contraindications, dosage, forms supplied, price and manufacturer's name and address. Names and addresses of Norwegian representatives of foreign manufacturers are also given. Cross-reference cards under names of common diseases list drugs used in the disease. Cards are revised periodically. Approximately 100 cards are issued each year. Four times a year new cards are distributed with a leaflet indicating additions and changes. Publisher's address: Sørligaten 8, Oslo.

Den Nordisk Veterinaer-forening Handbok. 1st ed. C. W. Cappelensvorlag, 1952. 508 pp. N. kr. 15.

Gives composition, indications and dosage. Arranged by indication.

Landbruks Departementek. **Dispensatorium Veterinarium Norvegicum 1951.** C. W. Cappelensvorlag, 1952. 89 pp. + Codex. N. kr. 6, 50.

Gives composition, action, dosage and preparations. Arranged alphabetically.

SWEDEN

Recepthandbok pa Grundval av de Nordiska Ländernas Farmakopeer, edited by Malte Ljungdahl. Malmö, Gleerups, 1953. 658 pp.

An alphabetic compilation by Latin names of drugs listed in the latest editions of all Scandinavian pharmacopeias and formularies. Entries include source of name, common or chemical name, description and properties, action, indications and dosage. Entries may be quite detailed, as in the case of *Benzylpenicillinum* and *Malonylkarbamider,* and lists of manufacturers with their specialty preparations are frequently appended. All drug names are included in the alphabetic general index.

Kungl. Medicinalstyrelsen. **M. B. 1950 (Samling av Benämningar 1950).** Stockholm, Nordiska Bokhandelns Förlag, 1950. 175 pp.

This formulary, issued by the Royal Medical Board, supplements the Swedish Pharmacopeia, providing a formulary of official preparations not in the Pharmacopeia. A new edition is announced for 1958. Address of Kungl. Medicinalstyrelsen: Vallingatan 2, Stockholm C.

Apotekens Kontrollaboratorium. **Apotekens Register över Standardforpackade Läkemedel 1956.** 20th ed. Stockholm, Viktor Pettersons Bokindustriaktiebolag, 1956. 528 pp. Sw. cr. 55, including supplements.

The *Register* is a comprehensive alphabetic list of pharmaceutical specialties and ACO drugs sold in Sweden. Entries give for individual drugs their composition, manufacturer, forms and sizes issued, price and, where applicable, classification as a poison or narcotic. Each drug is allotted an official registered number by which it is listed in a separate section, the *Synonymregister,* a classified pharmacologic list. Other sections list: roentgen contrast materials; biological preparations; manufacturers and local representatives of foreign manufacturers with their addresses; NFN (Nordisk Farmakopénaevn) names and names recommended by the World Health Organization with their chemical or common name equivalents. Products listed in the *Register* have been examined and released for sale by the Royal Medical Board and its pharmaceutical laboratory.

Supplements appear approximately monthly and the *Register* is revised annually. The 20th edition, 1957, has been announced. Address of Apotekens Kontrollaboratorium: Lindhagensgatan 128, Stockholm K.

Kungl. Medicinalstyrelsen. **Pharmaconomia Sveccia.** 3d ed. Stockholm, Nordiska Bokhandelns Förlag, 1956. 235 pp. Sw. cr. 19.25.

A handbook on drugs for physicians and medical students. Remedies are classed broadly by therapeutic activity. Individual entries give Latin name, Swedish name, composition, actions, indications, dosage and how supplied. Some trade-named preparations are included. It is revised approximately every five years. Address of Kungl. Medicinalstyrelsen: Vallingatan 2, Stockholm C.

Handkopsbenamningar (Retail Store Names), compiled by Gunnar Krook. Stockholm, Viktor Pettersons Bokindustriaktiebolag, 1951. 160 pp. Sw. cr. 13.

A one-volume alphabetical list of synonyms of official and unofficial drugs. The synonyms are arranged by Latin or Swedish name (common name). Names under which pharmaceutical preparations are known to the general public are included. Publisher's address: Fack, Stockholm 3.

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Correspondence about "Drug Information Sources" should be directed to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J.

SELECTED ABSTRACTS

Topical Use of Antibiotic Combination Following Surgery. Vaughn, A. M., Gliver, W. J., Martin, G., Annan, C. M., and Caserta, J. A. *Postgrad. Med. 21:*255 (1957). The use of local antibiotic therapy in the prophylaxis of post-operative infections has the advantage of permitting the control of even resistant localized infection by means of a high local concentration of the antibiotic without the development of side effects often observed from systemic therapy. The authors found this advantage to be attributable to a combination of tetracycline and neomycin. The combination was used in a series of 200 postoperative cases, including 49 laparotomies, 36 herniorrhaphies, 47 gynecologic procedures, and 56 miscellaneous operations. In this series the postoperative infection incidence was 3 per cent. In a similar series of 200 cases not given local treatment with the antibiotic combination, the incidence of postoperative infection was 10 per cent.

The antibiotic combination was used in five different dosage forms, as follows: (1) A non-adherent ointment dressing composed of a combination of a mixture of anhydrous cholesterol esters, bland hydrocarbon oils, and waxes emulsified with a dispersing agent. The base had a melting point of 42° C. and was impregnated in surgical gauze. One per cent of each antibiotic was incorporated in the base. The antibiotic was released over a prolonged period of time. (2) A nonirritating, absorbable powder composed of micropulverized betalactose with 2.5 per cent of each antibiotic in micropulverized form. (3) An absorbent dry packing composed of gauze impregnated with about 0.2 per cent of each antibiotic. (4) An ointment pack identical to the ointment dressing except for size. (5) An ointment spray dressing consisting of the ointment base homogenized and placed in an aerosol pressurized container with Freon as the propellent.

The particular applications of each of these dosage forms were discussed. The use and effectiveness of these dosage forms, containing tetracycline and neomycin, as means of controlling bacterial proliferation, facilitating healing and avoiding complications was emphasized.

The Effect of Antibiotic Combinations on Resistant Bacteria of Urinary Tract Origin. Clapper, W. E., and Sun, C. *Antibiot. and Chemother. 7:75* (1957). Strains of *Aerobacter aerogenes, Pseudomonas aeruginosa, Proteus* species and *Streptococcus faecalis* are frequently encountered in urinary tract infections, particularly after antibiotic therapy. The authors studied the effects *in vitro* of combinations of antibiotics on several resistant strains of these organisms isolated from clinical material. The antibiotics employed were penicillin, dihydrostreptomycin, polymyxin, chloramphenicol, oxytetracycline, tetracycline, erythromycin, and novobiocin.

The authors reported that 1 ug. of polymyxin with 10 ug. of tetracycline per ml. of medium rapidly killed more than 80 per cent of the Pseudomonas strains tested, although a definitely synergistic effect was observed on less than 50 per cent of the strains. This same combination killed only 25 per cent of the Aerobacter strains but, by increasing the concentration of polymyxin to 5 ug., 50 per cent were killed and a synergism was observed in the effect on 50 per cent of the strains.

The combination of 0.5 ug. polymyxin and 10 ug. chloramphenicol per ml. of medium killed 50 per cent of the strains of *Pseudomonas aeruginosa* and 55 per cent of the strains of *A. aerogenes,* while synergism was evident in 83 and 90 per cent, respectively. The combination of dihydrostreptomycin and novobiocin showed promise against resistant strains of Proteus and *S. faecalis.* However, further studies are necessary before definite results can be given.

The authors pointed out that the need for an effective combination of antibiotics against these strains of resistant bacteria is great. Resistant infections are frequently encountered in the urinary tract which will not respond to therapy with any of the currently known antibiotics alone.

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